Remarks

Claims 1-3, 6-13, 15-17, 19, and 20 are pending in the subject application. Applicants acknowledge that claims 4, 14, and 18 have been withdrawn from further consideration as being drawn to a non-elected invention. Applicants also gratefully acknowledge the Examiner's indication that claims 6, 16, 17, 19, and 20 are free of the prior art. By this Amendment, Applicants have canceled claims 2-7, 14, 17, and 18, amended claims 1, 8-13, 15, 16, 19, and 20, and added new claims 21-57. Support for the amendments and new claims can be found throughout the subject specification including, for example, at page 28, lines 29-32, and in the claims as originally filed. Applicants have also amended the "Cross-Reference to Related Applications" section of the subject specification to update the cross-reference to prior applications and have amended the subject specification to include a "government support" paragraph. In addition, Applicants have amended the title of the invention to correspond to amendments made to the claims. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1, 8-13, 15, 16, and 19-57 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicants note that a replacement sequence listing is being submitted in computer readable format and on paper with this Amendment. The replacement sequence listing includes sequences of the STAT1 and STAT3 binding sequences shown in Figure 1 of the subject specification that had not been provided in the prior sequence listing. The specification has been amended to include reference to appropriate SEQ ID numbers. I hereby certify that the paper and computer readable copies contain the same information and that no new material is added by this submission. Entry and consideration of the sequence listing is respectfully requested.

The specification is objected to on the grounds that it fails to comply with the requirements of 37 CFR 1.821 through 1.825. Specifically, the Examiner indicates that nucleic acid sequences are shown on pages 3-5 of the subject specification without including their corresponding SEQ ID numbers. By this Amendment, Applicants have amended the subject specification to include the SEQ ID NO. for the sequences shown at pages 3-5 of the specification. The specification is also objected to for a grammatical/typographical error on page 3, line 15. Applicants have amended page 3 of the subject specification to correct the inadvertent typographical error contained therein.

Applicants have also amended the subject specification to correct other miscellaneous typographical errors therein. Accordingly, reconsideration and withdrawal of the objections to the specification is respectfully requested.

The Examiner states that the Information Disclosure Statement (IDS) "filed 08/31/01 fails to comply with 37 CFR. 1.98(a)(2)." Specifically, the Examiner indicates that the references B, E, G-J, L, N, P, Q, Y, Z, and AA were not considered because a copy of the references was not provided with the IDS. Applicants are submitting herewith a Supplemental IDS with copies of references which were not available at the time the August 28, 2001 IDS was filed. Applicants respectfully request that the references cited in the Supplemental IDS be considered and made of record by the Examiner in the subject application.

Claims 3, 15, and 17 are objected to because of grammatical and typographical errors. Applicants have amended or canceled the claims, thereby rendering this objection moot. Reconsideration and withdrawal of the objection is respectfully requested.

Claims 9-12 are rejected under 35 USC §112, second paragraph, as indefinite. Applicants have amended claim 9 to correct the dependency such that claim 9 depends from claim 8. Applicants gratefully acknowledge the Examiner's careful review of the claims. Accordingly, reconsideration and withdrawal of the rejection under 35 USC §112, second paragraph, is respectfully requested.

Claims 1-3, 6-8, 13, 15-17, and 20 are rejected under 35 USC §112, first paragraph, as nonenabled by the subject specification. In addition, claims 1-3, 6-13, and 15-20 are rejected under 35 USC §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully assert that the claims are enabled by the subject specification and that there is adequate written description in the subject specification to convey to the ordinarily skilled artisan that they had possession of the claimed invention.

The Examiner does acknowledge under the rejection that the subject specification enables methods for inhibiting the function of a transcription factor in cell culture using the oligonucleotides of the invention. However, the Examiner asserts under the rejection that the subject specification does not enable *in vivo* treatment of whole organisms and that factors for the delivery of double

stranded transcription factor decoy (TFD) oligonucleotides parallel the unpredictabilities found in the art associated with antisense technology. In particular, the Examiner asserts that "there is a high level of unpredictability known in the antisense art for therapeutic, *in vivo* (whole organism) applications." Applicants respectfully assert that the use of double-stranded TFD oligonucleotides of the invention does not parallel those factors and barriers noted by the Examiner associated with antisense oligonucleotides. For example, Applicants respectfully assert that the oligonucleotides of the present invention can be successfully delivered to target cells, both *in vitro* and *in vivo*. Furthermore, antisense oligonucleotides, as the Examiner correctly points out, must hybridize in a sequence-specific manner with a target nucleic acid, whereas in the case of double-stranded TFD oligonucleotides of the invention, the transcription factors readily recognize the binding sequence presence on the TFD oligonucleotides. The Examiner also states in the Office Action that the "Discovery of antisense molecules with 'enhanced specificity' *in vivo* requires further experimentation for which no guidance is taught in the specification." The Examiner also quotes the Branch reference: "it is very difficult to predict what portions of an RNA molecule will be accessible *in vivo*, effective antisense molecules must be found empirically by screening a large number of candidates for their ability to act inside cells (Branch, p.49)." Applicants point out, however, that the oligonucleotides of the invention are not "antisense molecules." Thus, issues of antisense technology, *i.e.*, what portions of an RNA molecule will be accessible, *etc.* are not relevant to the oligonucleotides of the invention because they do not rely on nucleic acid hybridization but rather involve nucleic acid:protein binding. Thus, Applicants respectfully assert that the teachings in the Ma *et al.*, Jen *et al.*, Green *et al.*, Agrawal *et al.*, Branch and Bennett publications concerning antisense oligonucleotides are not directly applicable to the technology of the subject application and that oligonucleotides of the invention can be delivered and used to treat whole organisms *in vivo*.

However, by this Amendment, Applicants have amended the claims to delete references to "pharmaceutical" and "therapeutic" from the preamble of the claims, which the Examiner has indicated would overcome the rejection of the composition and agent claims. The methods of independent claims 1, 16, and 19 can be practiced *in vitro*. Applicants respectfully assert, however, that the claimed invention can be used in therapeutic and pharmaceutical applications. Applicants have also amended the independent claims to recite that the oligonucleotide comprises the sequence

TTCNNNGAA. Claim 1 has been amended to replace "modulating" with "inhibiting" the function of a transcription factor; Applicants note that the Examiner indicated in the Office Action that the specification enables "decreasing the function of a transcription factor . . .." Accordingly, in view of the above, Applicants respectfully assert that the claims are enabled and find adequate written description in the subject specification. Reconsideration and withdrawal of the rejections under 35 USC §112, first paragraph, is respectfully requested.

Claims 1-3 and 7 are rejected under 35 USC §102(b) as anticipated by Liu *et al.* (1997). In addition, claims 1-3 and 7 are rejected under 35 USC §102(a) as anticipated by Boccaccio *et al.* (1998). Claim 8 is rejected under 35 USC §103(a) as obvious over Liu *et al.* (1997) or Boccaccio *et al.* (1998) in view of Bard *et al.* (U.S. Patent No. 6,448,011). As a point of clarification, in regard to the Liu *et al.* reference, which appears to have been published in August of 1997, Applicants respectfully submit that the cited reference is not prior art to the subject application under §102(b) since the cited abstract was not published more than one year before the priority date of the subject application (July 30, 1998). In order to have been prior art under 35 USC §102(b), the Liu *et al.* reference would have to have been published before July 30, 1997.

Under all of the prior art rejections, the Examiner asserts that the Liu *et al.* reference is relied upon as teaching administration of a STAT 5 decoy to Dami/HEL and Meg-01 factor-independent leukemic cell lines and downregulation of the JAK2/STAT5 signaling transduction pathway. The Examiner indicates that the Boccaccio *et al.* reference teaches making an h-SIE decoy of the sequence which binds STAT and administration to MDCK, GTL 16, and MLP29 epithelial cell cultures for inhibition of the STAT transcription factor functions and decreasing growth of epithelial tubules. In the rejection under 35 USC §103, the primary references are relied upon as in the §102 rejection and the Bard *et al.* patent is cited as teaching "pharmaceutically acceptable carriers." Applicants respectfully traverse these rejections.

Applicants respectfully assert that the claimed invention is not anticipated by or obvious over the cited references. However, in a sincere effort to expedite prosecution of the subject application to completion, Applicants have amended the independent claims, as noted above, to include the oligonucleotide sequence limitation of claim 13, *i.e.*, TTCNNNGAA. Applicants note that the

Examiner has indicated in the outstanding Action that claim 13 is free of the prior art. Thus, all of the independent claims, as amended, and the claims dependent therefrom, are free of the prior art.

Accordingly, reconsideration and withdrawal of the rejections under 35 USC §§102 and 103 is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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DRP/sl
Attachments: New pages 1-3 (Sequence Listing) of the subject specification; Sequence Listing in computer readable format; Supplemental Information Disclosure Statement.